JACC Vol. 24, No. 1
July 1994:254–9

Quantification of Pericardial Effusions by Three-Dimensional Echocardiography

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Objectives. **The purpose of this study was to examine the accuracy of three-dimensional echocardiography for the quantification of asymmetric pericardial effusion volume and to compare this new technique with two-dimensional echocardiography.**

Background. **Quantification of pericardial effusion by two-dimensional echocardiography relies on a symmetric distribution of the fluid. Three-dimensional echocardiography can quantitate volume without these limitations, but its accuracy for pericardial effusion volume has not yet been assessed.**

Methods. **In six open chest dogs, 41 different asymmetrically distributed pericardial effusions of known volume were created by serial infusions of fluid through a pericardial catheter. The hearts were imaged using an automated echocardiographic method that integrates three-dimensional spatial and imaging data. The surfaces of the pericardial sac and heart were then reconstructed, and the volumes of pericardial effusions were calculated. Two-dimensional echocardiography was performed simultaneously, and volumes were calculated using the prolate ellipsoid method. Asymmetric distribution of the fluid was obtained by applying localized hydrostatic pressure to the pericardium.**

Results. **The volumes of pericardial effusion quantified using three-dimensional echocardiography correlated well with actual volumes ($y = 1.0x - 1.4$, SEE = 7.7 ml, $r = 0.98$). Two-dimensional echocardiography had an acceptable correlation ($y = 1.0x + 2.3$, SEE = 23 ml, $r = 0.84$), but a marked degree of variation from the true value was observed for any individual measurement.**

Conclusions. **Three-dimensional echocardiography accurately quantifies pericardial effusion volume in vivo, even when the fluid is distributed asymmetrically, whereas two-dimensional echocardiography is less reliable. This new technique may be of clinical value in quantitating pericardial effusion, especially in the serial evaluation of asymmetric or loculated effusions.**

(J Am Coll Cardiol 1994;24:254–9)

Although detection of pericardial effusions was one of the first applications of echocardiography (1,2), their accurate quantification has proved to be a more difficult challenge. Knowledge of not only the presence but also the volume of the effusion can assist in clinical decisions and has important prognostic value (3). In addition, accurate quantification of serial changes in pericardial effusion volume is critical when assessing pericardial disease or the need for use of drainage techniques. This is especially difficult when effusions are loculated or distributed asymmetrically.

Current echocardiographic methods to measure pericardial effusion volume assume that there is a uniform distribution and shape of the fluid collection (4–7). Because the distribution of the pericardial effusion within the pericardial space varies with the amount of fluid and the presence of loculations, the clinical application of quantitative two-dimensional methods has been limited.

Three-dimensional echocardiography can provide an accurate display of reconstructed cardiac structures in their proper spatial relations. It also allows accurate quantification of the size and volume of structures without the constraints of two-dimensional methods, which rely on formulas that assume a certain shape (8,9).

The purpose of this study was to determine the accuracy of three-dimensional echocardiography for the quantification of asymmetric pericardial effusions and to compare this new technique with two-dimensional echocardiography.

Methods

Experimental model. The protocol was approved by the Massachusetts General Hospital Research Subcommittee on Animal Care, and all dogs were maintained in accordance with the American Physiologic Society guidelines for care of

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Manuscript received November 8, 1993; revised manuscript received February 14, 1994, accepted February 25, 1994.

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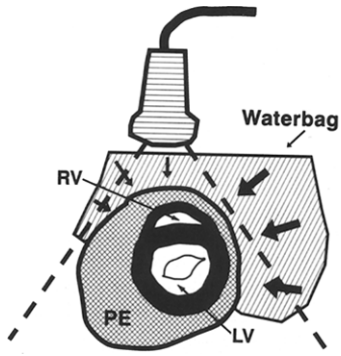

Figure 1. Creation of asymmetric effusion. A thin, flexible bag filled with saline solution is positioned over the pericardium, creating different degrees of pressure over the pericardial sac (arrows), resulting in asymmetric distribution of the fluid. LV = left ventricle; PE = pericardial effusion; RV = right ventricle.

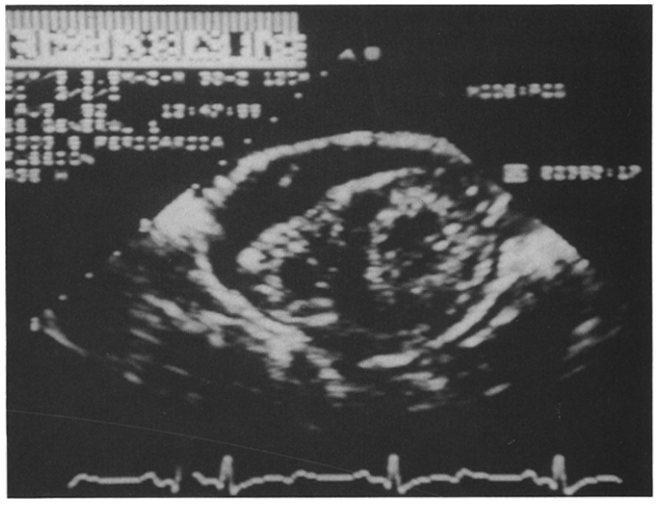

Figure 2. Two-dimensional echocardiographic short-axis view of a pericardial effusion with the corresponding three-dimensional positional data (digitally encoded in the upper left corner). Note the asymmetry of the effusion, which is predominantly anterior.

laboratory animals. Six mongrel dogs with a mean weight of 21.9 kg (range 16.0 to 28) were studied. The dogs were anesthetized with sodium pentobarbital (30 to 50 mg/kg body weight), intubated and ventilated mechanically. Central aortic pressure was monitored continuously and recorded. A median sternotomy was performed, and the parietal pericardium was exposed. A 5F catheter with side holes for infusion and an end hole for pressure measurement was advanced into the pericardial space. All pericardial fluid present was removed by aspiration through the catheter (range 2 to 10 ml), and the absence of pericardial fluid was confirmed by two-dimensional echocardiography. The entry site of the catheter in the pericardium was reinforced with purse-string sutures to prevent leakage between the catheter and the parietal pericardium.

Experimental protocol. At each stage, known volumes of warm saline solution were infused into or removed from the pericardial space through the catheter to create a series of pericardial effusions of known volume. In each dog, an average of seven volume stages was assessed. The volumes were infused and removed in random order, and the maximal volume infused in each pericardium was that at which the first signs of cardiac tamponade were observed. At each volume stage, three-dimensional echocardiographic imaging was performed. To obtain variable distributions of the effusions, a thin, flexible plastic bag filled with saline solution was positioned over the pericardial sac. By shifting the contents of this bag, different asymmetric distributions of the pericardial fluid around the heart were obtained (Fig. 1). This bag also served as a transducer standoff during echocardiographic imaging of the open chest preparation.

Three-dimensional echocardiography: data acquisition, reconstruction, display and quantification. Echocardiographic images were obtained using a commercially available phased-array scanner (Hewlett-Packard) and were recorded on ½-in. (1.27-cm) VHS videotape. A 3.5-MHz transducer was held on the transducer standoff, and intersecting long- and short-axis images were obtained. Using a previously described system (8,9), the position of the ultrasound image in space was determined with an acoustic locating device attached to the transducer and interfaced to a computer and the ultrasound machine. The spatial accuracy of this system has been demonstrated to be on the order of 0.1 mm (10). The positional data (Cartesian coordinates) were then encoded digitally and overlaid on an unused portion of the video signal that comes directly from the ultrasound machine (Fig. 2). The software allowed new spark gap positions to be updated in real time within the video refresh period of 33 ms. Thus each video frame has corresponding imaging, electrocardiographic (ECG) and spatial data. The goal of imaging was to obtain high quality images that included as much of the heart and pericardial space as possible. Although no specific image acquisition protocol was necessary, typically the parasternal imaging plane was used to depict the long axis of the cardiac structures and to scan continuously from the medial to lateral borders. Then the transducer was turned to obtain cross-sectional images approximating the short-axis planes from base to apex. The scan time necessary to acquire a complete set of images for the reconstruction was no longer than that needed for conventional two-dimensional imaging, typically <3 min.

For each of the experimental stages (i.e., each pericardial effusion volume), representative images were selected during videotape playback and digitized. Frames were selected carefully to include intersecting planes from the entire heart, to ensure inclusion of as many of the structures of interest as possible. Each time an image was digitized the locating data were automatically decoded and used to calculate the three-dimensional location of the image. Up to 27 frames could be accommodated by the computer algorithm; typically 20 to 23 images were digitized. To avoid mixing images from different

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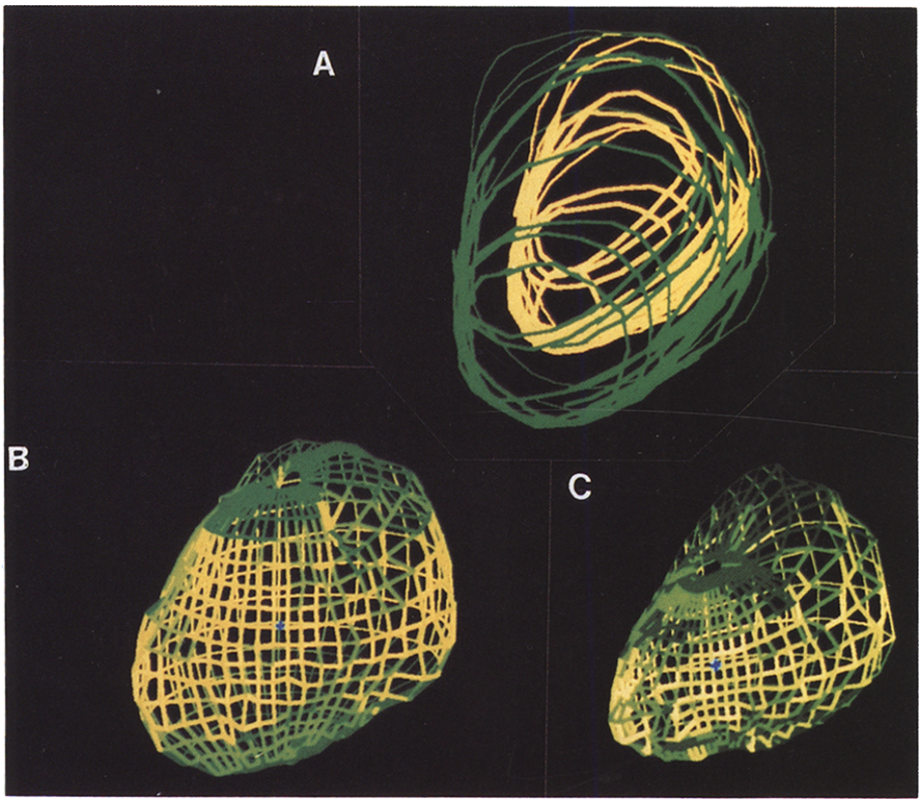


Figure 3. The volume of the pericardial effusion is obtained by subtraction of heart volume from pericardial sac volume. A, Three-dimensional orientation of the traces of the heart (yellow) and the pericardial sac (green). B, Rendering of the three-dimensional surface of the pericardial sac reconstructed from the green tracings in A. C, Surface rendering of the heart based on yellow tracings in A.

spatial positions due to heart motion during respiratory phases and different parts of the cardiac cycle, only images acquired during stable end-expiration, as determined by a respiratory marker recorded on the videotape, were used. All images selected were digitized at end-diastole (just after the QRS peak deflection on the simultaneous ECG).

The selected digitized images were then traced manually using a digitizing board (Summagraphics Inc.). The borders of the parietal pericardium and epicardium were traced at the same time in different colors. Tracing was performed by an observer who was unaware of the volume of pericardial effusion. Areas of lateral echo dropout or indistinct borders were not traced, as the computer algorithm is designed to tolerate incomplete or partial traces. As the images were traced they were oriented automatically in three-dimensional space (Fig. 3A). This enabled the operator to ensure that most portions of the heart and pericardium were included before surface rendering.

The surface of both the heart and pericardial sac were then reconstructed by a previously described automatic computer algorithm that provides a mathematical fit to the traced borders (11). This algorithm displayed the surface of the heart and the pericardial sac as a series of triangular patches. Contiguous tetrahedrons were then defined by connecting the end points of each of these surface triangles to the geometric center of the original traces. Volumes of the heart and pericardial sac were calculated by adding the volumes of the individual tetrahedrons. The pericardial fluid volume was derived from the difference of the two calculated volumes (Fig. 3).

The videotape review, image selection, tracing, surface reconstruction and volume calculation typically required 20 to 25 min per reconstruction of both the visceral and parietal pericardial surfaces.

Two-dimensional echocardiographic volume estimation. Standard two-dimensional parasternal short-axis and apical views of the heart were obtained at each pericardial effusion volume stage. Pericardial effusion volume was calculated using the method of D'Cruz et al. (7). This method assumes that the shape of the heart and pericardial sac are prolate ellipsoids. It requires one major (L) and two minor (D_1, D_2) axes of each structure to derive volumes by the formula: volume = $\pi \times 4/3 \times L/2 \times D_1/2 \times D_2/2$. Pericardial effusion volume is then the difference between pericardial sac volume and the volume of the heart. The major axis of the pericardial sac was measured in apical views from the superior wall of the sac (at the superior atrial wall) to the most apical extent of the parietal pericardium. The major axis of the heart was measured from the superior wall of the atria to the apical epicardium. The minor axes in the same apical view for both heart and pericardium were taken as their respective medial-lateral dimensions at the midventricular level. The remaining minor axes were taken as anteroposterior dimensions at the midventricular level in the short-axis view.

Data analysis. Pericardial effusion volumes calculated by three- and two-dimensional echocardiography were compared with true volumes using linear regression analysis. Differences between two regressions (standard errors of the estimate) were tested for significance using the F test. Because a wide range of values may yield a high correlation

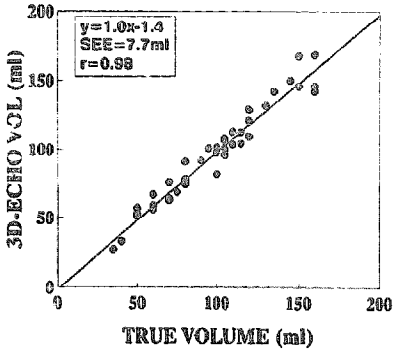


Figure 4. Correlation between pericardial effusion volume estimated by three-dimensional echocardiography (3D-ECHO VOL) and actual pericardial effusion volume.

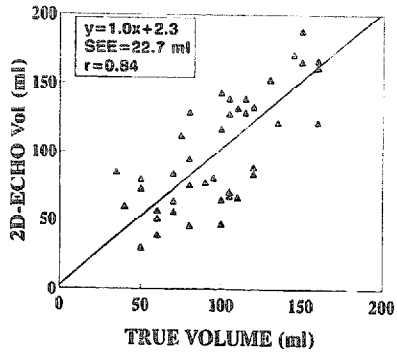


Figure 5. Correlation between pericardial effusion volume estimated by two-dimensional echocardiography (2D-ECHO Vol) and actual pericardial effusion volume.

coefficient even when data are in poor agreement, we also determined the mean difference between pairs of measurements (volume calculations and true values) according to the method described by Bland and Altman (12) and tested for significant differences between calculated and true volumes using a paired two-sample *t* test. Interobserver variability for digitization and tracing of images was expressed as the standard deviation of the differences between the measurements performed by two independent observers in 10 volume stages.

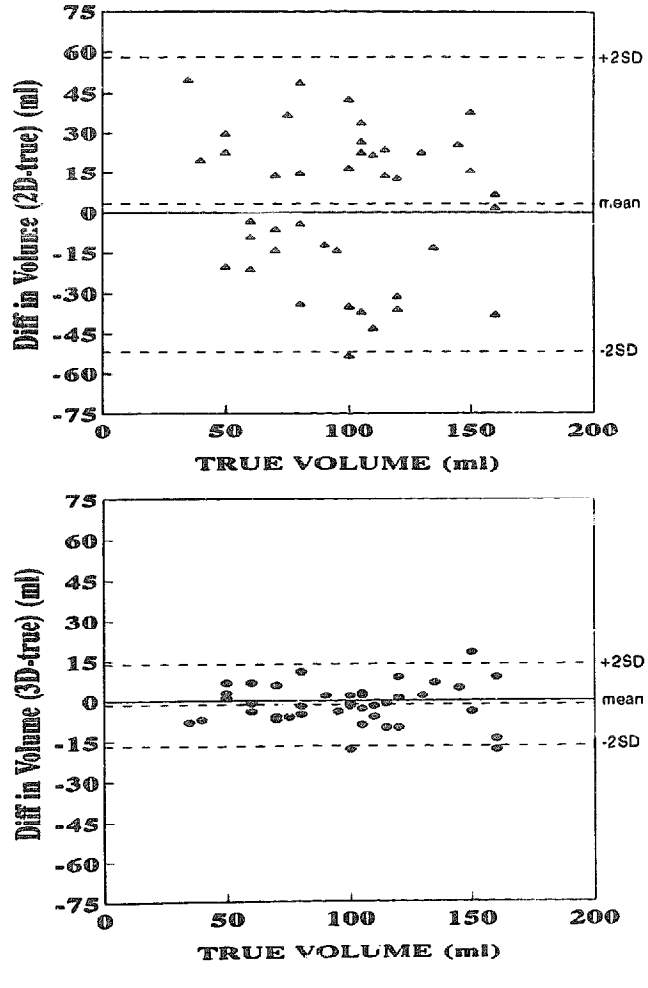
Results

Forty-one stages of pericardial effusion were studied, with volumes ranging from 35 to 160 ml. The fluid distribution was predominantly anteromedial in 37% and predominantly posterolateral in 63% of the stages. In all cases the three-dimensional reconstruction depicted the distribution of the effusion as created in the experiment and observed under direct visualization.

Pericardial effusion volume quantified using the three-dimensional echocardiography method correlated closely with the actual volume, as shown in Figure 4 ($y = 1.0x - 1.4$, SEE = 7.7 ml, $r = 0.98$). The agreement between three-dimensional echocardiographic assessment and actual volume was excellent. The mean error (mean difference) was 1.1 ± 7.8 ml (NS from 0). No systematic overestimation or underestimation of the true volumes was observed. Interobserver variability was 7.5 ml, or 6.5% of the mean.

Pericardial effusion volume estimated using the two-dimensional echocardiographic method also correlated well with the true values ($y = 1.0x + 2.3$, SEE = 22.7 ml, $r = 0.84$) (Fig. 5). Interobserver variability for the two-dimensional method was 10.5 ml, or 9.3% of the mean. The mean error (mean difference) was 3.6 ± 23 ml (NS from 0). Although there was no significant systematic error, the amount of scatter was significantly greater than with the three-dimensional method (F value 8.7, $p < 0.001$). The individual differences from true volume with the 95% confidence interval for both echocardiographic methods according to the Bland-Altman method are displayed in Figure 6.

Figure 6. Bland-Altman data analysis of two-dimensional (2D) (top) and three-dimensional (3D) (bottom) error. Diff = difference.



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Discussion

Echocardiography is a reliable and rapid noninvasive technique for the detection of pericardial effusion. Quantification of effusion volume is of additional clinical importance because knowledge of whether fluid collection is resolving or enlarging may provide information with regard to etiology and may influence patient management, such as assessment of the need for drainage (13).

This study demonstrates that experimentally created pericardial effusions can be displayed using three-dimensional echocardiography and that their volumes can be quantitated using this technique with greater accuracy than by the use of current two-dimensional echocardiographic methods.

Measurement of effusion volumes by echocardiography. Currently applied M-mode and two-dimensional echocardiographic methods for quantitating pericardial effusion volume assume that both the heart and pericardium conform to a specific shape, such as a sphere (4) or prolate ellipse (7). For the M-mode method, measurements are made in one dimension, whereas in the two-dimensional method, three segment lengths are measured at two levels of the heart. Thus, for maximal accuracy, such methods require a uniform distribution of the effusion (14,15) and the absence of distortion in the shape of the heart or pericardium. Therefore, when only the pericardial recesses contain fluid (16), when postural changes result in fluid shifts (5), when adjacent anatomic structures compress the pericardium and when intrapericardial adhesions result in loculation of fluid, the accuracy of these methods will be decreased. In addition, difficulties with proper image alignment and acquisition may also result in unreliable volume quantification. For example, to utilize the prolate ellipse formula properly, two orthogonal minor axes are required. This can be difficult because these two minor axes are measured from two different views. In fact, the commonly used mediolateral measurement from the apical four-chamber view and the anteroposterior measurement from the short-axis view rarely represent truly orthogonal planes. Inaccuracies in this method can also result if the true long axes of both the pericardium and heart are not measured correctly, due to foreshortening of the apical view.

Because of the manner in which quantification is performed, three-dimensional echocardiography demonstrates improved accuracy over earlier echocardiographic methods. As with the other echocardiographic methods, pericardial volume was derived from the difference between the pericardial sac volume and the volume of the heart. In contrast to the other methods, however, the volume calculations using three-dimensional echocardiography are based on images from all levels of the heart. The volume of each object was obtained using a versatile surfacing algorithm reconstructed at 800 grid points, which can account for regional irregularities or distortions in the shapes of both the heart and pericardium and avoids the need for geometric assumptions. In addition, the algorithm can handle discontinuous or incomplete data sets, so areas with indistinct borders do not have to be interpolated or extrapolated.

Advantages of three-dimensional echocardiography. The data from this study emphasize the important difference between correlation and accuracy. Both the two- and three-dimensional echocardiographic techniques demonstrated excellent linear correlations with true effusion volume. The variability in measurement for any individual volume, however, was three times larger for the two- than for the three-dimensional technique. Although two-dimensional echocardiographic methods can roughly estimate the amount of pericardial fluid, to measure the volume of fluid or its changes over time most accurately a more precise technique, such as three-dimensional echocardiography, is required.

Moreover, this model was designed specifically to recreate asymmetric distributions of fluid, mimicking the loculated effusions often observed in clinical practice. Such a model was chosen because it is precisely in this setting that the current M-mode and two-dimensional methods would be expected to be least accurate.

Clinical applications. The ability of three-dimensional echocardiography to quantitate small differences in effusion size may have useful clinical applications. Although most pericardial effusions resolve spontaneously, progressive fluid accumulation can lead to hemodynamic impairment and eventually require percutaneous or surgical drainage. In a recent study of 187 hospitalized patients with pericardial effusion (3), 9% had cardiac tamponade or required drainage. In that analysis, effusion size was found to be the most powerful predictor of tamponade. In clinical practice, knowledge of the size of the effusion and its evolution over time are particularly helpful for management decisions. Thus, the accurate quantification of effusion, as demonstrated in this study, might be used to guide management and the need for hospital admissions, as well as to determine the optimum timing for therapeutic procedures.

Technical considerations. The small errors in volume determination using three-dimensional echocardiography observed in this study appeared random because there was no systematic overestimation or underestimation of actual volume. These small differences between calculated and true volumes could be attributed to several technical sources of variability, including measurement of true volume, digitizing of images and tracing of borders. Attempts were made to limit these sources of variability. To ensure that the true volume was represented by the infused fluid, the pericardium was drained completely before starting the infusion of known volumes. To reduce variability in the tracing of borders, the middle of the bright echoes originating from the acoustic interfaces were traced consistently (17). Hopefully, the process of tracing structures will be even more consistent and less time-consuming with the development of automatic boundary detection systems. Because the reconstructed objects are the composite of tracings from multiple cardiac cycles, they will be affected by the motion of structures during respiration or changes in cardiac volume

due to changes in heart rate. We eliminated the respiratory motion by acquiring images during stable end-expiration. Care was taken to ensure that heart rate was uniform during each stage. Potential methods to improve control of these variables include gating data acquisition to phases of the respiratory cycle, averaging volumes acquired over several cardiac cycles and image acquisition during a single scan (18).

Echocardiographic imaging was performed in an open-chest model. Clearly, greater variability in the results can be expected in a clinical context, in which imaging quality may be less optimal than in this model. It is important to note, however, that 1) use of this model was necessary to validate the three-dimensional method against known pericardial volumes because complete volume recovery (particularly of viscous or cellular contents) is not generally possible in the clinical setting; and 2) echocardiographic imaging is often improved in patients with effusion because the fluid provides a larger and more direct window for ultrasound transmission.

Although the sizes of the effusions, ranging from 35 to 160 ml, were relatively small by human standards, the accuracy of the three-dimensional method in this more challenging situation and the independence of error from absolute volume (Fig. 6) suggest that relative accuracy should be better or at least as good for larger effusions. This study specifically investigated the accuracy of the technique for small loculated effusions.

Conclusions. In summary, three-dimensional echocardiography can accurately quantitate pericardial effusion volume, even in the case of asymmetric fluid distribution. The high degree of accuracy and precision of this new technique may be of great value for the assessment of serial changes in pericardial effusion volume. New technical developments in the area of digital gating and automatic border detection may enhance the applicability of this technique and contribute to its clinical utility.

We thank Tracy Svizzero for technical expertise with the experimental model and John B. Newell, BS, for helpful advice.

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